IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS :	Peled, *et al.*	**CONF. NO. :**	9770
SERIAL NUMBER :	10/774,843	**EXAMINER :**	Maria Gomez Leavitt
FILING DATE :	February 9, 2004	**ART UNIT :**	1633
FOR :	EXPANSION OF RENEWABLE STEM CELL POPULATIONS		

Via EFS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE

This paper responds to the April 30, 2010 Final Office Action. A response is due on or before July 30, 2010. Applicants believe no fees are due with this submission. However, the Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 24024-505 CON. A Notice of Appeal and the requisite fee is filed concurrently herewith.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks are shown starting on page 6 of this paper.

Listing of the Claims:

This listing of claims will replace all prior versions and listing of claims in the application:

1-400. (Cancelled)

401. (Currently Amended) A method of expanding a population of CD34+ hematopoietic stem cells *ex-vivo*, while at the same time, inhibiting differentiation of the stem cells *ex-vivo*, the method comprising:

(a) culturing said CD34+ hematopoietic stem cells *ex-vivo* under conditions allowing for cell proliferation, said conditions which comprise providing nutrients, serum and a combination of cytokines including each of stem cell factor, thrombopoietin, FLt3 ligand, and IL-6 and optionally IL-3 and,

(b) in the same culture medium providing nicotinamide in an amount between 1.0 mM to 10 mM,

wherein culturing said cells [are cultured] for a culture period of three weeks results [resulting] in expanding the population of CD34+ hematopoietic stem cells while inhibiting differentiation of said CD34+ hematopoietic stem cells *ex-vivo* to produce an expanded CD34+ hematopoietic stem cell population with an increased proportion of CD34+/Lin- and CD34+/CD38- cells in the expanded culture as compared to CD34+ cells cultured in the presence of cytokines and nutrients without exogenously added nicotinamide.

402-410. (Cancelled)

411. (Currently Amended) An isolated transplantable hematopoietic cell preparation comprising:

an expanded population of CD34+ hematopoietic stem cells propagated *ex-vivo* under conditions allowing for cell proliferation, said conditions which comprise providing a growth medium comprising nutrients, serum and a combination of cytokines including each of stem cell factor, thrombopoietin, FLt3 ligand, and IL-6 and optionally IL-3, and under conditions which inhibit differentiation, said conditions which comprise providing in said culture medium nicotinamide in an amount between 1.0 mM to 10 mM, wherein said isolated hematopoietic cell

preparation is characterized by a greater percentage of $CD34^+/CD38^-$ and $CD34^+/Lin^-$ cells after a three week culture period as compared to hematopoietic stem cells propagated in the presence of cytokines and nutrients without exogenously added nicotinamide; and a pharmaceutically acceptable carrier.

412 - 413. (Cancelled)

414. (Previously Presented) The method of claim 401, wherein said population of stem cells are selected from the group consisting of: embryonic stem cells and adult stem cells.

415. (Cancelled)

416. (Previously Presented) The method of claim 401, wherein said stem cells are derived from a source selected from the group consisting of: bone marrow, peripheral blood and neonatal umbilical cord blood.

417 - 418. (Cancelled)

419. (Previously presented) The method of claim 401, wherein said expanded hematopoietic cells are further characterized by an absence, or significantly diminished expression of cell surface antigens CD3, CD61, CD19, CD33, CD14, CD15 or CD4.

420 - 421. (Cancelled)

422. (Previously Presented) The method of claim 401, wherein said combination of cytokines further comprise at least one cytokine selected from the group consisting of: interleukin-1, interleukin-2 interleukin-10, interleukin-12 and tumor necrosis factor-α.

423. (Previously Presented) The method of claim 401, which method further comprises providing late acting cytokines.

424. (Original) The method of claim 423, wherein said late acting cytokines are selected from the group consisting of: granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor, erythropoietin, FGF, EGF, NGF, VEGF, LIF, Hepatocyte growth factor and macrophage colony stimulating factor.

425 - 436. (Cancelled)

437. (Cancelled).

438. (Cancelled).

439 - 463. (Cancelled)

464. (Previously presented) The method of claim 401, wherein said culturing said cells in the presence of said exogenously added nicotinamide is for a period of up to three weeks.

465. (Previously presented) The isolated transplantable cell preparation of claim 411, wherein said culturing said cells in the presence of said exogenously added nicotinamide is for a period of up to three weeks.

466 - 468. (Cancelled)

469. (Previously presented) The method of claim 401, wherein said cells are cultured in the presence of 1.0 mM of exogenously added nicotinamide.

470. (Previously presented) The method of claim 401, wherein said cells are cultured in the presence of 5.0 mM of exogenously added nicotinamide.

471. (Previously presented) The method of claim 401, wherein said cells are cultured in the presence of 10.0 mM of exogenously added nicotinamide.

472 - 477. (Cancelled)

478. (Previously presented) The transplantable cell preparation of claim 411, wherein said cells are propagated in the presence of 1.0 mM of exogenously added nicotinamide.

479. (Previously presented) The transplantable cell preparation of claim 411, wherein said cells are propagated in the presence of 5.0 mM of exogenously added nicotinamide.

480. (Previously presented) The transplantable cell preparation of claim 411, wherein said cells are propagated in the presence of 10.0 mM of exogenously added nicotinamide.

481. (Cancelled)

REMARKS

Claim Amendments

Upon entry of this amendment, claims 401, 411, 414, 416, 419, 422-424, 464-465, 469-471 and 478-480 will be pending in the application.

Independent Claims 401 and 411 have been amended to recite that the culture medium includes each of stem cell factor, thrombopoietin, FLt3 ligand, and IL-6 and optionally IL-3. Support for this amendment is found throughout the specification (*See, e.g.* page 25, lines 24-28). Claims 401 and 411 have also been amended to recite that the observed greater percentage of $CD34^+/CD38^-$ and $CD34^+/Lin^-$ cells can be observed after a three week culture period. Support for this amendment can be found in Example 5 of the specification as filed.

No new matter is added. The amendments to the claims are solely for the purpose of clarity and do not require the Examiner to conduct a new search – thus, applicant requests that these claim amendments be entered.

The Claims Are Not Obvious over Brown in View of Block

There is a single outstanding obviousness rejection in this case – the Examiner has rejected the claims over a combination of Brown (US Publication 2002/0159984) in view of Block (US 6,413,772). Applicants traverse.

On page 3 of the Office Action, the Examiner contends that the phrase "a combination of cytokines including stem cell factor, thrombopoietin, FLt3 ligand, IL-6 and optionally IL-3" can be construed to permit any combination of the recited cytokines. Applicants disagree. However, so there can be no doubt, applicants have amended the claims to make crystal clear that the growth conditions require each of stem cell factor, thrombopoietin, FLt3 ligand, and IL-6 (and optionally IL-3). Brown simply does not teach that the use of these four required cytokines together in the presence of nicotinamide within the claimed range will produce hematopoietic cell populations with a greater percentage of $CD34^+/CD38^-$ and $CD34^+/Lin^-$ cells after a three week culture period. In fact, Brown is fatally deficient -- Brown shows exactly the opposite result. Figure 3 of Brown clearly demonstrates that after Day 14, the percentage of $CD34^+/CD38^-$ cells declines (whether in the presence or absence of serum). For this reason alone, the obviousness rejection fails.

The Examiner has also dismissed the February 2010 Declaration of Dr. Tony Peled, allegedly on the ground that no statistical analysis was presented. The statements in paragraphs 4 and 5 are evidence of record that cannot be ignored -- Applicants reiterate those conclusions here. Specifically, Dr. Peled's February 2010 Declaration stated that her data:

> "demonstrates that culturing in a growth media including stem cell factor, thrombopoietin, FLt3 ligand and IL-6 in the presence of serum and nicotinamide results in a cell population that is expanded in the population of CD34+ hematopoietic stem cells with an increased proportion of CD34+/Lin- and CD34+/CD38- cells in the expanded culture as compared to CD34+ cells cultured in the presence of cytokines and nutrients without exogenously added nicotinamide." February 2010 Decl. Of Dr. Peled, ¶ 4.

For the avoidance of doubt, Applicants have also submitted a further Declaration of Dr. Tony Peled under 37 CFR §1.132 ("July 2010 Peled Decl.") which sets forth data confirming that the specifically claimed combination of cytokines produces an expanded CD34+ hematopoietic stem cell population with an increased proportion of CD34+/CD38- and CD34+/Lin- cells in the expanded culture as compared to CD34+ cells cultured in the presence of those cytokines and nutrients without exogenously added nicotinamide (as expressly recited in independent claims 401 and 411 – and thus all the claims that depend therefrom). Furthermore, Dr. Peled's July 2010 Declaration makes crystal clear that the results are statistically significant. In addition, the Examiner is directed to Example 5 of the specification as filed which provides further evidence of the unexpected results obtained according to the claimed methods and cell populations obtained thereby.

The combination of Brown and Block teaches away from the claimed invention. The Examiner concedes that Brown is fatally deficient in failing to disclose the claimed range of nicotinamide concentration. Brown does not suggest to the skilled artisan that the claimed nicotinamide concentration range in serum free media can act as an agent that maintains CD34+ hematopoietic cells in an undifferentiated state and enriches for CD34+/CD38- and CD34+/Lin- cells while the cells are expanded in *ex vivo* culture using a serum-containing culture medium – as claimed here.

Block does not cure the deficiencies of Brown – Block teaches away. Block refers to the use of nicotinamide in the culture/expansion of differentiated hepatocytes – a completely different cell population than the claimed CD34+ hematopoietic stem cell population. Further, none of the cytokines recited in instant claims are present in the Block culture medium. And the ordinarily skilled artisan would not select (out of the many "ingredients" in Block's culture

medium) nicotinamide for use as claimed here. To the contrary, Block teaches the exact opposite – in Block, nicotinamide was used to maintain the differentiated state of the hepatocytes (exactly opposite to the use in the currently claimed invention). *See*, Block, col. 8, lines 26-28. Block also directly teaches away from the use of serum in the culture – as expressly recited in the claims here. The entire focus of Block is to provide a chemically defined culture medium that is serum free. *See*, *e.g.*, col. 1, lines 43-50 and col. 4, lines 8-10.

Applicants reiterate the statement in their February 22, 2010 Response, that hepatocytes are a completely different cell population from undifferentiated CD34+ hematopoietic stem cells. Block discloses the use of nicotinamide for maintaining differentiated hepatocytes in culture. Here the invention recites methods and compositions of cell that are enriched for undifferentiated cells (as evidenced by the increased proportion of CD34+/Lin- cells and the increased proportion of CD34+/CD38- cells in the culture) after 3 weeks in the presence of the recite dcytokines and nictinamide. That is the opposite to the teachings of Block.

One of ordinary skill in the art combining the teachings of Brown and Block would not, and could not, reach the present invention with predictable results.

The data presented herewith in the July 2010 Peled Decl. and in both previously submitted February 2010 Peled Decl. (see specifically ¶¶ 4-6, Figures 1 and 2) and 2008 Peled Declaration (pages 2-4 and Figure 1) shows that using nicotinamide in the range of 1.0 mM to 10 mM, as required by the instant claims inhibits differentiation of $CD34^{+}$stem cells (as evidenced by the unexpectedly and substantially increased cell density of undifferentiated CD34+/CD38- and CD34+/Lin- cells), while permitting expansion, *ex vivo*. These unexpected and superior properties are not taught or suggested by the prior art.

CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested. However, if upon receipt and review of this amendment, the Examiner believes that the present application is not in condition for allowance and that changes can be suggested which would place the claims in allowable form, the Examiner is respectfully requested to call Applicant's undersigned counsel at the number provided below.

Respectfully submitted,

/ Matthew Pavao /

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Dated: July 30, 2010

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Peled et al.	CONF NO.:	9770
SERIAL NUMBER:	10/774,843	EXAMINER :	Maria Gomez Leavitt
FILING DATE:	February 9, 2004	ART UNIT :	1633
FOR:	EXPANSION OF RENEWABLE STEM CELL POPULATIONS		

Via EFS
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Alexandria, VA 22313-1450

DECLARATION OF DR. TONY PELED UNDER 37 C.F.R. §1.132

I, Tony Peled, declare and state that:

1. I received a Ph.D. degree from the Hebrew University - Hadassah Medical School in Jerusalem, Israel. I am the Chief Scientist, Vice President and co-founder of Gamida Cell Ltd. of Jerusalem, Israel (the Assignee of the above-referenced application). A principal aspect of my research is the study of stem cell culture and the therapeutic application of stem cell technology. I am the author of numerous peer-reviewed publications and posters, most of which are directed to cell expansion and cell differentiation, with specific focus on hematopoietic stem cells.

2. I have reviewed the Final Office Action dated April 30, 2010. I understand that claims 401, 411, 414, 416, 419, 422-424, 464, 465, 469-471 and 478-480 are rejected under 35 U.S.C. § 103(a) as being unpatentable over US Patent Publication No. 2002/0159984 to Brown ("Brown") over U.S. Patent No. 6,413,772 to Block ("Block").

3. I have reviewed the accompanying amendment and the above-referenced application in conjunction with the cited references.

4. I assert that CD34+ hematopoietic stem cells of the instant invention are cultured *ex-vivo* under conditions allowing for cell proliferation. These conditions require providing

nutrients, serum, and a combination of cytokines including each of stem cell factor, thrombopoietin, FLt3 ligand and IL-6. The CD34+ hematopoietic stem cells of the present invention can also be cultured under these conditions and further include IL-3.

5. The data accompanying this declaration shows the effect of nicotinamide (NAM) in $CD34^+$ cells derived from umbilical cord blood during 3 weeks in cultures supplemented with cytokines (each of FLT3, IL-6, TPO, and SCF). Analysis included the number of total nucleated cells (TNC), colony forming unit cells (CFUc) and phenotypic characterization of hematopoietic progenitors, $CD34^+$ and $CD34^+CD38^-$ cells.

6. Figure 1 accompanying this declaration shows cord blood-derived purified $CD34^+$ cells cultured for 3 weeks with cytokines (each of FLT3, IL-6, TPO, and SCF) or with cytokines (each of FLT3, IL-6, TPO, and SCF) and nicotinamide ("NAM") at 2.5 and 5 mM. Each bar represents the average ± SE of 4 independent experiments.

7. Panel A-E shows the analysis of cultured cells one week post seeding.

8. Panel A shows the number of total nuclear cells (TNC) (*$P<0.01$ vs. NAM, 2.5 and 5 mM).

9. Panel B shows the number of $CD34^+$ cells (*$P<0.008$ vs. NAM).

10. Panel C shows representative FACS analysis dot plots of cells double stained with CD34 PE and CD38 FITC.

11. Panel D shows percentages of $CD34^+CD38^-$ cells (*$P<0.01$ vs. NAM non-treated cultures).

12. Panel E shows the numbers of $CD34^+CD38^-$ cells (*$P<0.03$ vs. NAM non-treated cultures).

13. To track cell division history, freshly purified $CD34^+$ cells were labeled with PKH2, cultured and analyzed 7 day post seeding. Histograms of PKH fluorescence intensity of $CD34^+$ (Panel F) and $CD34^+CD38^-$ (Panel G) cells are shown. The histograms present the same number of cells for both control and NAM-treated cells in a representative experiment out of three experiments performed.

14. Panel H shows the median fluorescence intensities of NAM expanded cells on day 7 cultures of three separate experiments as percentages of control cultures treated with cytokines alone.

15. Panel I shows the percentages of $CD34^{+}CD38^{-}$ cells, one, two and three weeks post seeding (*$P \leq 0.01$ vs. NAM non-treated cultures). Panels J-L show the fold expansion (FE) of TNC (*$P<0.01$ vs. NAM, **$P<0.03$ vs. NAM 5mM) (J), CFUc (*$P<0.03$ vs. NAM, **$P<0.02$ (K) and $CD34^{+}$ cells (*$P \leq 0.01$ vs. NAM) (L), one, two and three weeks post seeding.

16. Figure 2 accompanying this declaration shows cord blood derived purified CD34+ cells cultured with cytokines, with and without NAM (2.5-5mM) and FACS analyzed after 3 weeks as following: cells were count and thereafter stained with FITC-conjugated antibodies against differentiation antigens (CD38, CD33, CD14, CD15, CD3, CD61, CD19) and with PE-conjugated antibodies against CD34. Positive PE and negative FITC cells were considered as CD34+Lin- cells. The results show the actual number in culture of CD34+CD38- Lin- cells calculated from the total number of cells. Each experiment was repeated with cells derived from 6 different cord blood units.

17. The data accompanying this declaration shows, as early as one week post seeding, that the number of total nuclear cells (TNC) (Fig. 1A) and $CD34^{+}$ cells (Fig. 1B) were substantially lower, while percentages (Fig.1C-D) and absolute number (Fig. 1E) of $CD34^{+}CD38^{-}$ cells were significantly higher in cultures treated with 2.5 and 5 mM NAM as compared with control cultures treated with cytokines only. The divisional history of seeded $CD34^{+}$ cells stained with PKH indicated that during the first week in culture, the vast majority of $CD34^{+}$ cells underwent several cycles under both culture conditions (Fig. 1F-G), with consistent lesser divisions (higher fluorescence intensity) of cells cultured with NAM (Fig. 1H). Slower cycling was particularly prominent in the $CD34^{+}CD38^{-}$ subset (Fig. 1G) which, nevertheless, increased within the expanded cell population from week one through week-3 (Fig.1I). After three weeks in culture, fold expansion of TNC (Fig. 1J), CFUc (Fig. 1K) and $CD34^{+}$ cells (Fig. 1L) in NAM-treated reached the values in NAM non-treated cultures. Phenotype characterization of lineage differentiated cells in three week cultures revealed lessening of differentiation in cultures treated with NAM (2.5 and 5 mM) than in cultures treated with

cytokines alone, as demonstrated by significant lower percentages of CD14, CD11b, CD11c and $CD15^+$ cells (Fig. 2).

18. Thus, it is shown that $CD34^+$ cells cultured with NAM displayed an initial slower proliferation rate than their counterparts cultured without NAM. This was most pronounced in the putative HPC compartment defined as $CD34^+CD38^-$ cells, along with an increase in their numbers in the presence of NAM. Our results demonstrate that culturing with each of FLT3, IL-6, TPO, and SCF in the presence of NAM produced an expanded CD34+ hematopoietic stem cell population with an increased proportion of CD34+/Lin- and CD34+/CD38- cells in the expanded culture as compared to CD34+ cells cultured in the presence of those cytokines and nutrients without exogenously added nicotinamide.

19. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that willful false statements may jeopardize the validity of this application and any patent issuing therefrom.

A. P.
Tony Peled, Ph.D.

Signed this 30 day of July, 2010

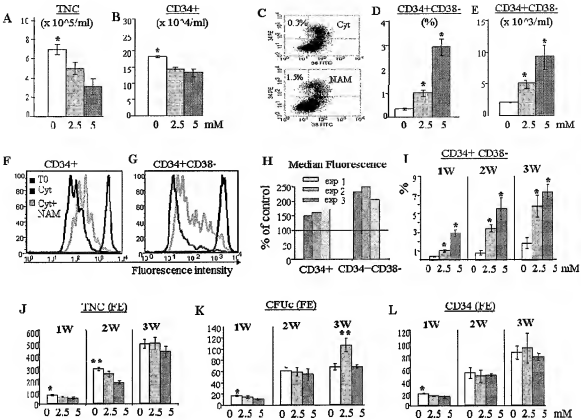

Fig.1

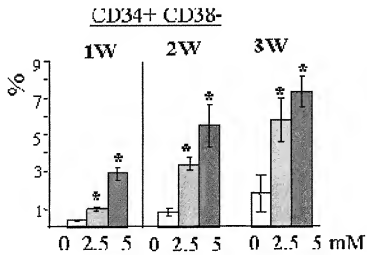

Figure 1

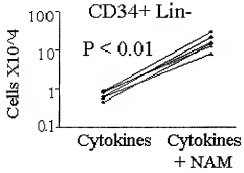

Figure 2

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,843	02/09/2004	Tony Peled	24024-505 CON	9770

30623 7590 08/17/2010

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EXAMINER	
LEAVITT, MARIA GOMEZ	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
08/17/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/774,843	PELED ET AL.	
	Examiner	Art Unit	
	MARIA LEAVITT	1633	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 30 July 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *401,411,414,416,419,422-424,464,465,469-471 and 478-480*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Maria Leavitt/
Primary Examiner, Art Unit 1633

Continuation of 3. NOTE: Amended claim 401 and 411 introduce specific limitations, i.e., "wherein culturing said cells for a culture period of three weeks" and "after a three week culture period", respectively. These limitations were not previously examined requiring new search and consideration of the art made of record, and of the specification for support of the amendment. Therefore, the amendment to the claims filed on 02-11-2010 has not been entered..

Continuation of 11. does NOT place the application in condition for allowance because: Applicants' arguments have been considered, but they are based on the declaration signed by Dr. Tony Peled. A declaration after-final is not considered unless it is specifically directed to a new rejection first made in a final office action, thus the declaration filed on 07-30-2010 and signed by Dr. Tony Peled has not been entered. The declaration is specifically directed to rejection of claims 35 U.S.C. 103(a) as being unpatentable over Brown R (US Publication No. 2002/0159984, Date of Publication October 31, 2002) over Block et al., (US Patent 6,413,772, Date of Patent July 2, 2002) (see page 7 of Applicants' remarks). .